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3Serial No. 10/052,547

3Response to Office Action of 3/26/04

3Amendment

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The following list of claims will replace all prior versions of the claims in the application:

1. (*Canceled*)

2. (*Currently amended*) A method for assessing toxicity ~~and toxicology~~ of a compound <u>of interest</u>, comprising:

    a) exposing <u>tissue samples comprising</u> a set of genes to ~~a~~ <u>the</u> compound <u>of interest</u>;

    b) ~~monitoring the response~~ <u>measuring the hybridization signal</u> of each gene in the set of genes to the compound <u>of interest</u>;

    c) creating gene expression profiles using two or more variables<u>, wherein the two or more variables include time and dose</u>;

    d) creating composite variables from the gene expression profiles of (c);

    e) creating one composite from the composite variables of (d); and

    f) comparing the results of (e) to a profile of a known compound <u>to determine whether there is a toxicological response to the compound of interest</u>.

3. (*Previously added*) The method of Claim 2, wherein the set of genes comprises 10-100,000 genes.

4. (*Currently amended*) The method of Claim 2, wherein the <u>two or more</u> variables ~~are time,~~ <u>further include</u> treatment ~~or dose~~.6

6. (*Previously added*) The method of Claim 2, wherein <u>step (b) further comprises averaging</u> the ~~response~~ <u>hybridization signals</u> of the genes ~~is averaged</u> <u>to determine a background level; and</u>

       <u>selecting for further analysis the hybridization signals that exceed a pre-selected percentage of the background level</u>.

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7. (*Previously amended*) The method of Claim 2, wherein step (c) comprises performing contrast analysis.

8. (*Previously amended*) The method of Claim 2, wherein step (c) comprises performing cluster analysis.

9. (*Previously amended*) The method of Claim 2, wherein step (d) comprises performing principal components analysis.

10. (*Currently amended*) The method of Claim 2, wherein the composite variables of (e) are created using logistic regression[,] or discriminant analysis.

11. (*Currently amended*) A method for screening a compound of interest for toxicological effect, comprising:

(a) selecting a plurality of polynucleotide targets wherein the polynucleotide targets have a first gene expression levels altered in ~~tissues~~ a first tissue sample treated with known toxicological agents;

(b) treating a second tissue sample with a the compound ~~to be tested~~ of interest to induce second gene expression levels of a the plurality of polynucleotide targets; and

(c) comparing the first expression ~~level~~ levels of (a) with the second expression ~~level~~ levels of (b) to generate a measure of similarity;

wherein the measure of similarity is indicative of toxicological effect of the compound of interest.

12. (*Canceled*)

13. (*Previously added*) The method of Claim 11, wherein the tissue samples are liver, kidney, brain, spleen, pancreas and lung.

14. (*Previously added*) The method of Claim 11, wherein the known toxicological agent is acetaminophen.

15. (*Previously added*) The method of Claim 11, wherein the known toxicological agent is CCl₄.

16. – 22. (*Canceled*)

23. (*Previously added*) The method of Claim 2, wherein step (d) comprises performing partial least squares analysis.

24. (*Previously added*) The method of Claim 2, wherein step (d) comprises performing factor analysis.

25. (*Currently amended*) The method of Claim ~~1~~ 2, wherein the compound of interest is acetaminophen.

26. (*Currently amended*) A method for assessing the toxicity ~~and toxicology~~ of a compound of interest, comprising:

a) exposing tissues comprising a set of genes to ~~a~~ the compound of interest;

b) generating gene expression data corresponding to the ~~response~~ hybridization signal of each gene in the set of genes to the compound of interest;

c) selecting a subset of the gene expression data which are time stable and dose dependent;

d) combining the subset of gene expression data into one or more composite variables to assign each gene to a pattern; and

e) converting the one or more composite variables into one predictive composite measure for determining a probability of similarity;

wherein the ~~one predictive measure~~ probability of similarity comprises an indicator of toxicological effect of the compound of interest.

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27. (*Previously added*) The method of claim 26, wherein step (c) comprises performing contrast analysis.

28. (*Previously added*) The method of claim 26, where step (d) comprises performing principal components analysis.

29. (*Previously added*) The method of claim 28, wherein step (e) comprises performing a logistic regression using the principal components identified in step (d).

30. (*New*) The method of claim 26, wherein the tissue samples are liver, kidney, brain, spleen, pancreas and lung.

31. (*New*) The method of claim 26, wherein step (b) further comprises averaging the hybridization signals of the genes to determine a background level, and wherein the gene expression data is generated from the hybridization signals that exceed a pre-selected percentage of the background level.

32. (*New*) The method of Claim 2, wherein the tissue samples are liver, kidney, brain, spleen, pancreas and lung.

33. (*New*) The method of Claim 2, wherein the compound of interest is CCl_4.